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**Lung cancer stem cells: progress and prospects.**

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**Public Summary:**

Epithelial stem cells are critical for tissue generation during development and for repair following injury. In both gestational and postnatal stages, the highly branched and compartmentalized organization of the lung is maintained by multiple, resident stem/progenitor cell populations that are responsible for the homeostatic maintenance and injury repair of pulmonary epithelium. Though lung epithelial injury in the absence of oncogenic mutation is more commonly expressed as chronic lung disease, lung cancer is the most common form of death worldwide and poses a highly significant risk to human health. Cancer is defined by the cell of origin, responsible for initiating the disease. The Cancer Stem Cell Hypothesis proposes that cancer stem cells, identified by stem-like properties of self-renewal and generation of differentiated progeny, are responsible for propagating growth and spread of the disease. In lung cancer, it is hypothesized that cancer stem cells derive from several possible cell sources. The stem cell-like resistance to injury and proliferative potentials of bronchioalveolar stem cells (BASCs) and alveolar epithelial type II cells (AEC2), as well as cells that express the cancer stem cell marker glycoprotein prominin-1 (CD133) or markers for side populations make them potential reservoirs of lung cancer stem cells. The abnormal activation of pathways that normally regulate embryonic lung development, as well as adult tissue maintenance and injury repair, including the Wnt, Hedgehog (Hh) and Notch pathways, has also been identified in lung tumor cells. It is postulated that therapies for lung cancer that specifically target stem cell signaling pathways utilized by lung cancer stem cells could be beneficial in combating this disease.

**Scientific Abstract:**

Epithelial stem cells are critical for tissue generation during development and for repair following injury. In both gestational and postnatal stages, the highly branched and compartmentalized organization of the lung is maintained by multiple, resident stem/progenitor cell populations that are responsible for the homeostatic maintenance and injury repair of pulmonary epithelium. Though lung epithelial injury in the absence of oncogenic mutation is more commonly expressed as chronic lung disease, lung cancer is the most common form of death worldwide and poses a highly significant risk to human health. Cancer is defined by the cell of origin, responsible for initiating the disease. The Cancer Stem Cell Hypothesis proposes that cancer stem cells, identified by stem-like properties of self-renewal and generation of differentiated progeny, are responsible for propagating growth and spread of the disease. In lung cancer, it is hypothesized that cancer stem cells derive from several possible cell sources. The stem cell-like resistance to injury and proliferative potentials of bronchioalveolar stem cells (BASCs) and alveolar epithelial type II cells (AEC2), as well as cells that express the cancer stem cell marker glycoprotein prominin-1 (CD133) or markers for side populations make them potential reservoirs of lung cancer stem cells. The abnormal activation of pathways that normally regulate embryonic lung development, as well as adult tissue maintenance and injury repair, including the Wnt, Hedgehog (Hh) and Notch pathways, has also been identified in lung tumor cells. It is postulated that therapies for lung cancer that specifically target stem cell signaling pathways utilized by lung cancer stem cells could be beneficial in combating this disease.

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